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| EXAMINER | |
|---|---|
| OGUNBIYI, OLUWATOSIN A | |

| ART UNIT | PAPER NUMBER |
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| 1645 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com
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Patent_Mail@arentfox.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/529,654 | VEDRINE ET AL. | |
| | Examiner | Art Unit | |
| | OLUWATOSIN OGUNBIYI | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/31/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Claims 1-20 are pending in the application. Claims 1-17 are under examination.

***Election/Restrictions***

Applicant's election with traverse of Group I in Paper No. 20080804 (mailed 8/19/08) is acknowledged.

Applicants traverse the restriction as it may be applicable to amended claim 1.

The traversal is on the ground(s) that Pyle *et al.* disclose a method for detecting and counting, which is not based on an inducible enzymatic activity (i.e., respiration) and certainly not glycosidases, esterases, phosphatases and sulfatases. Moreover, Pyle *et al.* disclose a method for detecting and counting, which method does not use any enzymatic substrate to be cleaved by said enzymatic activity. In fact, the Pyle *et al method* only uses fluorescent antibodies. These distinctions over Pyle *et al.* enable the method of the invention to detect and count specific microorganisms with a great sensibility and specificity.

This is not found persuasive because the technical feature of Group I as amended c is obvious over Berg et al. WO 89/04372, 18th May 1989 (cited in IDS) in view of Pyle et al WO 95/31481 23 November 1995 (cited in IDS). The technical feature of Group I is drawn to:

a method for detecting and counting the microorganisms in a sample comprising the steps of:

a) selectively enriching the microorganism sought in the sample,

b) inducing or activating at least one enzymatic activity of the aforementioned microorganism,

c) immunomagnetically concentrating the enzymatically activated microorganism,

d) fluorescently labeling the concentrated microorganism obtained after immunomagnetic concentration is carried out by adding to the medium containing the aforementioned microorganism at least one substrate comprising one part specific to the enzymatic activity to be indicated and one label part, the transformation of the substrate takes

place inside the aforementioned microorganism and that the fluorescent product is retained in the aforementioned microorganism, and
e) detecting and analyzing the fluorescence making possible the
numeration or counting of the microorganisms sought is carried out by fluorescence microscopy or filtration cytometry or fluorescence microscopy.

Berg et al teaches a method of assaying a dilute concentration of living pathogenic microorganisms in a sample of product for human consumption, comprising contacting a sample comprising microorganisms e.g. bacteria with a nutrient medium capable of supporting the metabolism and reproduction of the microorganisms (selectively enriching the microorganisms sought in the sample), inducing the production of an enzyme in said microorganism by contacting said microorganism with an agent such as lactose that is capable of inducing the production of an enzyme (specific to the microorganism sought) in said microorganism (inducing or activating at least one enzymatic activity), then contacting by adding to the media containing the enzymatically induced microorganism a fluorogenic substrate which reacts with the enzyme to release the fluorescent portion thereof (label part), and adding a permeability agent which increases the permeability of the microorganisms to the enzyme or fluorogenic substrate or both and incubating the cells to permit contacting of the enzyme (whether inside or outside the microorganism) with the fluorogenic substrate and the release of the fluorescent portion of the fluorogenic substrate. Berg et al teaches a step wherein the amount of fluorescence emitted is calculated and the concentration of microorganisms is determined by counting the number of fluorescent microclonies (fluorescence microscopy). See p. 6 -7, p. 9 lines 14-15 and p. 21-22 claim 1.

Berg et al does not teach immunomagnetically concentrating the enzymatically activated microorganism before the fluorescent labeling of the microorganism.

Pyle et al teaches a method for detection and enumeration of viable microorganisms in a sample. Pyle et al also relies on a metabolic indicator and uses immunomagnetic separation/concentration using antibodies which specifically binds to a target bacteria to concentrate the bacteria before addition of a metabolic indicator and before detection of fluorescence. See p. 38 lines 1-29. Pyle et al teaches that immunomagnetic separation is a widely used method for facilitating concentration and separation from samples (p. 38 lines 30 to p. 40) and that immunomagnetic capture not only permits cell concentration but also the selection of a specific antigenic cell type. See p. 41 lines 7-19.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have immunomagnetically concentrated the enzymatically induced microorganisms of Berg et al before addition of the fluorogenic substrate in order to concentrate a specific antigenic cell type in the sample prior to the fluorescent labeling and counting as taught by Pyle et al (p. 38 lines 30 to p. 40) who teaches that immunomagnetic capture not only permits cell concentration but also the selection of a specific antigenic cell type), thus resulting in the instant invention with a reasonable expectation of success.

The restriction requirement between Groups I and II is still deemed proper for the reasons above and is therefore made FINAL.

Claims 18-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 20080804 in the reply filed 9/15/2008.

As to the species election, Applicants elect the species of fatty acid with traverse in the reply filed 1/12/09. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

However, upon further consideration, the species election requirement is ***withdrawn***.

***Priority***

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

***Specification***

The abstract of the disclosure is objected to because of the use of legal phraseology such as "said". Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

***Information Disclosure Statement***

The information disclosure statement filed 5/31/05 has been considered. An initialed copy is enclosed.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 step d) the recitation of *by adding to the medium containing the aforementioned microorganism* lacks antecedent basis in the claim as the previous steps do not

indicate that the microorganisms are in a medium. Also, in step d) *the transformation of the substrate takes place inside the aforementioned microorganism and that the fluorescent product is retained in the aforementioned microorganism*, the claim does not clearly indicate how the substrate is transformed and does not indicate that the substrate has a fluorescent precursor thus *the fluorescent product* lacks antecedent basis in the claim.

Claims 4 and 7, *conditioning step* lacks antecedent basis as claim 1 does not recite a *conditioning step*.

Claim 8 (a) and (b), *conditioning medium or medium* lacks antecedent basis as claim 1 does not recite a *conditioning medium or a medium*.

As to claim 5 and 6, the recitation of *can be carried out simultaneously* or *can take place* renders the claims indefinite because *can* indicates a possibility and does not indicate that Applicants are definitively claiming that step a and step b *is* (as opposed to *can*) carried out simultaneously in claim 5 or step c) takes place before step b) or step c) takes place after step d). The use of *can* indicates that claim 5 or 6 is an option. If Applicant intends this to be so, please clarify on the record.

In claim 6, it is confusing how step c take place before step b. Step c requires immunomagnetically concentrating the enzymatically activated microorganism. Step b requires inducing or activating at least one enzymatic activity of the enriched microorganism. If step c takes place before step b, then at what point is the microorganism of step c enzymatically activated. As claimed, step c before step b would result in a missing step and lack of antecedent basis for the enzymatically activated microorganism of step c.

In claim 6, it is confusing how step c can take place after step d. Step c requires immunomagnetically concentration the enzymatically activated microorganism. Step d requires fluorescently labeling the concentrated microorganism. If Step c occurs after step d, when and how is the microorganism of step d then concentrated? As claimed, step c after step d would result in a missing step of concentrating the microorganisms of step d and lack of antecedent basis for the concentrated microorganism of step d.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is

followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 17 recites the broad recitation for porosity size between 0.2 and 10 um and the claim also recites *preferably* between 0.2 and 5um and 0.2 and 0.5 um which are the narrower statements of the range/limitation. A narrower range or preferred range may be set forth in another independent claim or in a dependent claim.

Also, the term *approximately 2g/L* or *approximately 5000 u/L* in claim 2 or *approximately 10g/L* in claim 7 or *approximately 63 microns* in claim 16 is a relative term which renders the claim indefinite. The term *approximately* is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In claim 2, for catalase, the metes and bounds of the concentration set forth is not clear. The unit *μ/L* is not a unit of concentration. The *μ* (micro) is not a unit of mass, thus it is not clear what concentration of catalase is being set forth in claim 2.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 6, 11, 14, 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. WO 89/04372, 18th May 1989 (cited in IDS) in view of Pyle et al WO 95/31481 23 November 1995 (cited in IDS).

The claims are drawn to a method for detecting and counting the microorganisms in a sample comprising the steps of:

a) selectively enriching the microorganism sought in the sample,

b) inducing or activating at least one enzymatic activity of the aforementioned microorganism,

c) immunomagnetically concentrating the enzymatically activated microorganism,

d) fluorescently labeling the concentrated microorganism obtained after immunomagnetic concentration is carried out by adding to the medium containing the aforementioned microorganism at least one substrate comprising one part specific to the enzymatic activity to be indicated and one label part, the transformation of the substrate takes place inside the aforementioned microorganism and that the fluorescent product is retained in

the aforementioned microorganism, and
e) detecting and analyzing the fluorescence making possible the
numeration or counting of the microorganisms sought is carried out by fluorescence microscopy.

Berg et al teaches a method of assaying a dilute concentration of living pathogenic microorganisms in a sample of product for human consumption, comprising contacting a sample comprising microorganisms e.g. bacteria with a nutrient medium capable of supporting the metabolism and reproduction of the microorganisms (selectively enriching the microorganisms sought in the sample), inducing the production of an enzyme in said microorganism by contacting said microorganism with an agent such as lactose that is capable of inducing the production of an enzyme (specific to the microorganism sought) in said microorganism (inducing or activating at least one enzymatic activity), then contacting by adding to the media containing the enzymatically induced microorganism a fluorogenic substrate which reacts with the enzyme to release the fluorescent portion thereof (label part), and adding a permeability agent which increases the permeability of the microorganisms to the enzyme or fluorogenic substrate or both and incubating the cells to permit contacting of the enzyme (whether inside or outside the microorganism) with the fluorogenic substrate and the release of the fluorescent portion of the fluorogenic substrate. Berg et al teaches a step wherein the amount of fluorescence emitted is calculated and the concentration of microorganisms is determined by counting the number of fluorescent microclonies (fluorescence microscopy). See p. 6 -7, p. 9 lines 14-15 and p. 21-22 claim 1.

As to claim 5, Berg et al teaches that selectively enriching the microorganism and inducing or activating the enzymatic activity can be carried out simultaneously since Berg et al teaches that the microorganisms are initially contacted with an actuating medium that comprises 1) the nutrient media or selectively enriching the microorganism and 2) the production agent e.g. lactose. See p. 6 lines 5-15.

As to claim 11, Berg et al teaches that the fluorescent labeling of the microorganism is carried out by adding to said actuating media the fluorogenic substrate which comprises a substrate part specific to said enzymatic activity and a fluorescent label part (e.g. fluorogenic substrates: 4-methylumbeliferone-heptanoate p. 7 lines 19-24, or 4-methylumbeliferone-beta-D-galactoside, p. 14 line 20-25, wherein cleavage by induced enzymes reveals fluorescent 4-methylumbeliferone). See p. 6 lines 5-15.

As to claim 15 and 17, Berg et al teaches that the sample can be filtered before commencing on the steps of detecting and counting the microorganism e.g. see p. 12 0.2 um to 0.8um pore size, p. 14 example 1 lines 11-14 using filter pore size 0. 045 um, p. 19 lines 8-10.

Berg et al does not teach immunomagnetically concentrating the enzymatically activated microorganism before the fluorescent labeling of the microorganism, and does not teach immunomagnetically concentrating the microorganisms before inducing enzymatic activity.

Pyle et al teaches a method for detection and enumeration of viable microorganisms in a sample. Pyle et al also relies on a metabolic indicator and uses immunomagnetic separation/concentration using antibodies which specifically binds to a target bacteria to concentrate the bacteria before addition of a metabolic indicator and before detection of fluorescence. See p. 38 lines 1-29. Pyle et al teaches that immunomagnetic separation is a widely used method for facilitation concentration and separation from samples (see p. 38 lines 30 to p. 40) and that immunomagnetic capture not only permits cell concentration but also the selection of a specific antigenic cell type. See p. 41 lines 7-19.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have immunomagnetically concentrated the enzymatically induced microorganisms of Berg et al before addition of the fluorogenic substrate in order to concentrate a specific antigenic cell type in the sample prior to the fluorescent labeling and counting as taught by Pyle et al (p. 38 lines 30 to p. 40) who teaches that immunomagnetic capture non only permits cell concentration but also the selection of a specific antigenic cell type), thus resulting in the instant invention with a reasonable expectation of success.. As to claim 6, it would have been prima facie obvious in said method of Berg et al to immunomagnetically concentrate the microorganisms in the sample before the enriching step or enzyme induction (immunomagnetic concentration before induction or activation of enzymatic activity) or delaying the addition of the fluorogenic substrate to the medium until after immunomagnetic concentration, so as to concentrate a specific antigenic cell type in said sample of Berg et al, thus resulting in the instant invention with a reasonable expectation of success. Pyle et al teaches that immunomagnetic capture/concentration not only permits cell concentration but also the selection of a specific antigenic cell type (see p. 41 lines 7-19) and there would have been a reasonable expectation of detecting and counting microorganisms irrespective of when specific antigenic type of microorganism is concentrated or captured from the sample.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. WO 89/04372, 18th May 1989 and Pyle et al WO 95/31481 23 November 1995 as applied to claims 1, 4,5,6, 11, 14, 15 and 17 above, further in view of Sigma catalog 1996 p. 2179-2181.

The combination of Berg and Pyle is set forth supra. Said combination does not teach a filtration step before a), b) c), d) and e) using a filter whose porosity size is 20-100 microns.

Sigma catalog teaches filters with various porosity size (retention size) including between 20-25 and 30 microns. See p. 2181.

Since the combination of Berg and Pyle et al teach detection of microorganisms in water comprising sewage effluent or raw domestic sewage (see Berg et al, example 1, p. 1), it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to filter the water sample containing sewage using a filter with large pore size e.g. 20-25 or 30 microns or larger (see Sigma catalog p. 2181) to remove any particulate matter prior to enriching microorganisms in the sample, thus aiding the detecting and counting process and resulting in the instant invention with a reasonable expectation of success.

Claims 8, 9, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. WO 89/04372, 18th May 1989 and Pyle et al WO 95/31481 23 November 1995 as applied to claims 1, 4, 5, 6, 11, 14, 15 and 17 above, further in view of Olsen et al. Plant and Soil 186:75-79, 1996.

The combination of Berg and Pyle is set forth supra. Said combination does not teach (claim 8) that the immunomagnetic concentration step comprises a) placing the microorganism sought, present in the conditioning medium, in contact with an antibody directed against an antigen specific to the microorganism, the aforementioned antibody being conjugated with a magnetic bead, b) separating the bead-antibody-microorganism complexes from the medium, and c) separating the microorganism from the rest of the complex; does not teach (claim 9) a method according to claim 8, wherein the antibody conjugated with a magnetic bead is directed against an antibody that is itself directed against an antigen specific to the microorganism sought; does not teach (claim 10) a method according to claim 8

or 9, wherein the magnetic beads have a diameter that is between 1 and 20 um, or between 2 and 8 um.

Olsen et al teaches a method of detecting and counting the number of bacteria in sample using immunomagnetic concentration before detecting and counting of the concentrated cells by fluorescence microscopy. See p. 77 column 1 and column 2 figure 2. The immunomagnetic procedure uses magnetic beads that are 2.8 um in diameter, p. 76 column 2 under immunomagnetic beads, and comprises contacting the bacteria in the sample with an antibody directed against the bacteria, separating the bead antibody bacteria complexes from the medium and separating the microorganism from the rest of the complex by vortexing to detach the beads and separation of the beads via magnetization (see p. 77 column 1 under analytical procedure). Said magnetic bead also comprises a secondary antibody that is directed to the antibody that is directed to the bacteria, which aids in detection of the bacteria.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to carry out the immunomagnetic concentration step of Berg et al and Pyle et al as combined using the known immunomagnetic concentration guideline set forth in Olsen et al which involves contacting the bacteria in the sample with an antibody directed against the bacteria being sought, separating the bead antibody bacteria complexes from the medium and separating the microorganism from the rest of the complex by vortexing to detach the beads and separation of the beads via magnetization procedure and using magnetic bead comprising a secondary antibody that is directed to the antibody that is directed to the bacteria, which aids in detection of the bacteria, (see p. 77 column 1 under analytical), thus arriving at the instant invention with a reasonable success. The combination of Berg et al and Pyle et al teach a method of detecting and counting bacteria in a sample using the combination of immunomagnetic separation and fluorescence microscopy and Olsen et al also teaches a method of detecting and counting the number of bacteria in sample using immunomagnetic concentration band detecting and counting of the concentrated cells by fluorescence microscopy, it would have been prima facie obvious to adapt the general immunomagnetic concentration protocol set forth in Olsen et al and tailor said protocol for the immunomagnetic concentration step in Berg and Pyle et al as combined as both immunomagnetic concentration techniques are essentially accomplishing the same thing i.e. concentration of a specific antigenic type of bacteria from a sample.

Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. WO 89/04372, 18th May 1989 and Pyle et al WO 95/31481 23 November 1995 as applied to claims 1, 4,5,6, 11, 14, 15 and 17 above, further in view of Boyd et al US 5,510,243 Apr. 23 1996.

The combination of Berg and Pyle is set forth supra. Said combination does not teach the use of a monosaccharide substrate part specific to the enzymatic activity to be revealed and does not teach that the fluorogenic label is a xanthene.

Boyd et al teaches the method of detecting bacteria *E. coli* and discriminating between said *E. coli* and non-target bacteria using fluorogenic substrates such as fluorescein-di-beta-D-galactopyranoside which has a label part that is a xanthene i.e. fluorescein and a substrate part (di-beta-D-galactopyranoside) comprising a monosaccharide which is specific to Beta-galactosidase enzyme and Boyd et al teaches the use of galactosidase inducers e.g. IPTG to include in media comprising the *E. coli* to be detected. See column 3 line 14-16, 50 to 667 to column 4 lines 1-6 and 60- 67.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to substitute the fluorogenic substrate (which comprises a substrate part and label part) and the enzymatic inducer of the combination of Berg and Pyle with another fluorogenic substrate and inducer known in the art for detection of bacteria in a sample such as fluorescein-di-beta-D-galactopyranoside which has a label part that is a xanthene i.e. fluorescein and a substrate part (di-beta-D-galactopyranoside) comprising a monosaccharide which is specific to Beta-galactosidase enzyme and the galactosidase inducer e.g. IPTG (see Boyd et al column 3 line 14-16, 50 to 67 to column 4 lines 1-6 and 60- 67), thus resulting in the instant invention with a reasonable expectation of success. It is prima facie obvious to substitute known fluorogenic substrate and inducer systems as they are similarly used for the same thing i.e. detecting bacteria in a sample.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. WO 89/04372, 18th May 1989 and Pyle et al WO 95/31481 23 November 1995 as applied to claims 1, 4, 5, 6, 11, 14, 15 and 17 above, further in view of Kaclikova et al. Journal of Microbiological Methods, Vol. 46 Issue 1 July 2001, p. 63-67.

Berg and Pyle et al as combined is set forth supra. The combination does not teach addition of yeast extract to the enrichment medium.

Kaclikova et al teaches a method of detecting *Listeria* in a product for human consumption (cheese) using enrichment media (Fraser broth) and immunomagnetic separation. See p. 63 column 2 lines 1-3 and p. 64. under section 2.4. Half-Fraser broth comprises amongst other things yeast extract 5g/L[1].

Since the combination of Berg and Pyle is drawn to detection and counting of pathogenic microorganisms in a sample of product for human consumption (see abstract of Berg et al), it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to modify the enrichment media of Berg and Pyle as combined by adding nutrients for enriching and detecting other pathogenic microorganisms in products for human consumption such as *Listeria*. Kaclikova et al teaches a method of detecting Listeria in food samples (see title). Said nutrients include those contained in Half-Fraser enrichment broth for detecting of Listeria which comprises yeast extract (see Kaclikova et al p. 63 column 2 lines 1-3 and p. 64. under section 2.4., thus resulting in the instant invention with a reasonable expectation of success.

[1]Technical Bulletin for Fraser Listeria Enrichment Broth Base: for the selective enrichment of Listeria in the 2-step method acc. to D.G.AL. and ISO 11290-1 (1996). EMD Merck KGaA, Damstadt, Germany, 2002.
http://www.emdchemicals.com/analytics/Micro_Manual/TEDISdata/prods/1_10398_0500.html. Retrieved, March 9, 2009.

***Status of Claims***

Claims 1-17 are rejected. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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